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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/031,496	01/14/2002	William S. Adney	NREL 99-45	6834
23712	7590	02/28/2005	EXAMINER	
PAUL J WHITE, SENIOR COUNSEL NATIONAL RENEWABLE ENERGY LABORATORY (NREL) 1617 COLE BOULEVARD GOLDEN, CO 80401-3393			PATTERSON, CHARLES L JR	
		ART UNIT		PAPER NUMBER
				1652

DATE MAILED: 02/28/2005

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)
	10/031,496	ADNEY ET AL.
	Examiner Charles L. Patterson, Jr.	Art Unit 1652

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --
Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) Responsive to communication(s) filed on 26 November 2004.
- 2a) This action is **FINAL**. 2b) This action is non-final.
- 3) Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) Claim(s) 6-18 is/are pending in the application.
 - 4a) Of the above claim(s) _____ is/are withdrawn from consideration.
- 5) Claim(s) _____ is/are allowed.
- 6) Claim(s) 6-18 is/are rejected.
- 7) Claim(s) _____ is/are objected to.
- 8) Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

- 9) The specification is objected to by the Examiner.
- 10) The drawing(s) filed on 28 November 2004 is/are: a) accepted or b) objected to by the Examiner.
 Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
 Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

- 12) Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
 - a) All b) Some * c) None of:
 1. Certified copies of the priority documents have been received.
 2. Certified copies of the priority documents have been received in Application No. _____.
 3. Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).
- * See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

- | | |
|---|---|
| 1) <input checked="" type="checkbox"/> Notice of References Cited (PTO-892) | 4) <input type="checkbox"/> Interview Summary (PTO-413) |
| 2) <input type="checkbox"/> Notice of Draftsperson's Patent Drawing Review (PTO-948) | Paper No(s)/Mail Date. _____. |
| 3) <input type="checkbox"/> Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08)
Paper No(s)/Mail Date _____. | 5) <input type="checkbox"/> Notice of Informal Patent Application (PTO-152) |
| | 6) <input type="checkbox"/> Other: _____. |

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35 U.S.C. 101 reads as follows:

Whoever invents or discovers any new and useful process, machine, manufacture, or composition of matter, or any new and useful improvement thereof, may obtain a patent therefor, subject to the conditions and requirements of this title.

Claims 6-18 are rejected under 35 U.S.C. 101 because the claimed invention is not supported by either a specific and substantial asserted utility or a well established utility. This rejection is repeated for essentially the reasons given in the last action. Applicants arguments have been carefully considered but do not overcome the instant rejection.

Applicants argue that page 1, lines 25-33 discussed the "problem addressed by Applicant [which] was to provide genetic mutations that mitigate the problems that arise when the *T. reesei* CBH1 is expressed in a heterologous host...[i.e.] increasing the thermal tolerance of CBH1". As stated in the previous action, although applicants disclose the various genetic manipulations in great detail they do not disclose the results of these manipulations. The examiner has re-read the instant specification and does not find any teaching that any mutant has increased thermal tolerance. The specification teaches that rCBH I N270A has activity in *A. awamori*, but the thermal tolerance of that mutant is not disclosed and furthermore none of the claims is limited to this embodiment. In the absence of any results as to what these manipulations produce there does not appear to be a specific and substantial asserted utility for them.

Claim 6-18 also rejected under 35 U.S.C. 112, first paragraph. Specifically, since the claimed invention is not supported by either a specific and substantial asserted utility or a well established utility for the reasons set forth above, one skilled in the art clearly would not know how to use the claimed invention.

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Claims 12-18 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the enablement requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention.

The instant claims are drawn to replacing the N-glycosylating amino acid that "includes asparagine together with surrounding amino acid residues as encoded by at least one of SEQ ID NO. 20, 21, and 22 and the replacement residue includes alanine together with surrounding amino acid residues as encoded by at least one of SEQ ID, NO. 83, 85, and 87" and to SEQ ID NO:20, 21 and 22 and combinations thereof. One of ordinary skill in the art would not know exactly what the claim was referring to. Looking at the sequence disclosure, SEQ ID NO: 20, 21 and 22 apparently do not contain a codon for asparagine and SEQ ID NO: 83 and 87 apparently do not contain a codon for alanine. SEQ ID NO:85 contain "ccc" (the codon for Ala) at positions 8-10 but there is no indication in any of the sequences what the reading frame of the sequences is. There is apparently no indication in the specification where SEQ ID NO:20-22, 83, 85 or 87 are located in the *cbhl* gene, which is supposedly shown in SEQ ID NO:4. In applicants Remarks in the instant amendment it is stated that "[t]he positional reference [to Asn 45, 270 or 384] was made to the translated amino acid sequence of the catalytic domain as shown in Fig. 1 and SEQ ID NO:4 (emphasis added). This explanation is not seen in the specification as filed. Furthermore, looking at the regions surrounding these positions in the catalytic domain, SEQ ID NO:20-22, 83, 85 or 87 is not seen. Therefore the ordinary artisan would not know specifically where to make these mutations.

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Claims 12 and 15-18 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claim 12 is incorrect in the recitation of "SEQ ID NO." on line 4 and "SEQ ID, NO." on line 6. The correct recitations are "SEQ ID NO:". The claim is also incorrect in the recitation of "residue includes" on line 5, which should apparently be "residues include".

Claims 15-17 are indefinite and confusing in the recitation of "sequence change encoded by SEQ ID NO:20 [21, 22]". Applicants state that the claims "have been amended to clarify that what is being claimed is a sequence change" and have amended the claims to read "encoded by" instead of "of". However, "sequence change" still implies that there was some starting sequence that was then changed, and the instant claim do not indicate what sequence was changed to what. From the amendment to claim 12, SEQ ID NO:20-22 appear to be the sequences that are encoded before the sequence change.

Claim 18 is confusing and indefinite in the recitation of "exoglucanases selected form the group consisting of claims 15, 16 and 17". "Claims 15, 16 and 17" are not exoglucanases but rather define exoglucanases. Changing the recitation to read "exoglucanases selected form the group consisting of the exoglucanases of claims 15, 16 and 17" or some similar recitation would overcome this rejection. The claim is also indefinite in that it does not state what combination of claims 15-17 the composition is. This reads on 7 compositions, each of the exoglucanases of claims 15-17, all 3 of the exoglucanases and all of the combinations of 2.

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The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

A person shall be entitled to a patent unless -

(b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

Claims 17 and 18 are rejected under 35 U.S.C. 102(b) as being anticipated by either of Nakari, et al. (A or B) or Fowler, et al. (C). The two Nakari references teach an exoglucanase comprising SEQ ID NO:22 in SEQ ID NO:17 from residues 336-359. Fowler, et al. teach an exoglucanase comprising SEQ ID NO:22 in SEQ ID NO:9 from residues 269-292.

Claims 11-14 are rejected under 35 U.S.C. 103(a) as being unpatentable over Godbole, et al. (U). This rejection is repeated for the reasons given in the last action. Applicants arguments have been carefully considered but do not overcome the instant rejection.

As previously stated, the instant reference teaches that when the *Trichoderma reesei cbh1* gene is transformed into *Pichia pastoris*, the rCBH I enzyme produced is overglycosylated and has less activity than the wild type CBH I enzyme produced by *Trichoderma reesei*. In fact it is taught that "Pichia species are known to overglycosylate heterologous proteins". Since the

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only difference in the enzyme is the glycosylation level, one of ordinary skill in the art would conclude that the activity of the CBH I enzyme from *T. reesei* is reduced by having too much glycosylation and one very obvious way to reduce glycosylation is to reduce the number of residues that can be glycosylated. Applicants argue that the examiner is engaging in the "obvious to try" standard and that "'obvious to try' is not the standard of obviousness, and the reference actually teaches away from doing what the Office now asserts is obvious" citing the passage in column 1 of page 833. The examiner does not agree with this characterization. The reference teaches unambiguously that over-glycosylation of CBH I causes it to loose activity. As to the cited passage on page 833, the stated purpose of the research in the instant reference is to "attempt to produce active, wild-type-like CBH I from *P. pastoris*" so that "the thermal tolerance of *T. reseii* CBH I [can be increased] by protein engineering (last sentence of Introduction and first sentence of the second paragraph of the Introduction, respectively). Therefore the recitation on page 833 that "these forms of rCBH I are not appropriate for structure-based enzyme engineering" refers to the greatly reduced activity seen with this wild-type enzyme in this host. The fact remains that the reference teaches that overglycosylation of CBH I decreases activity. It would have been obvious to one of ordinary skill in the art that if an active CBH I was desired in a eukaryotic host, the glycosylation could be reduced by reducing the number of residues that could be glycosylated.

Claims 6 and 8 are rejected under 35 U.S.C. 103(a) as being unpatentable over Srisodsuk, et al. (V). This rejection is repeated for the reasons given in the last action. Applicants arguments have been carefully consi-

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dered but do not overcome the instant rejection. The instant reference teaches at least in the abstract that deletion of about 1/3 of the linker region of CBH I reduces the binding but does not affect its enzymatic activity on cellulose, whereas a longer deletion reduces the rate of cellulose degradation even though the enzyme still binds to the substrate. It is concluded that sufficient spatial separation of the core form the cellulose binding domain is required for efficient functioning of CBH I. It is further taught in the introduction that "[t]he linkers identified in *T. reesei* cellulases are approximately 30-44 amino acids in length". Therefore, it would have been obvious to one of ordinary skill in the art that a linker region was required for significant activity against cellulose. It would have been further obvious that if the linker was reduced to 24 nucleotides, the mutated enzyme would have significant activity in view of the teachings of the instant reference.

Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a). It is noted that applicants changed the identity of the sequences, necessitating some of the instant rejections.

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the

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advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Charles L. Patterson, Jr., PhD, whose telephone number is 571-272-0936. The examiner can normally be reached on Monday - Friday from 7:30 to 4:00.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Ponnathapura Achutamurthy, can be reached on 571-272-0928. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).



Charles L. Patterson, Jr.
Primary Examiner
Art Unit 1652

Patterson
February 16, 2005